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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,300	12/12/2005	Jean-Paul Rene Marie Andre Bosmans	PRD2061USPCT	2524

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
06/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@woodcock.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,300	BOSMANS ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-13* is/are pending in the application.

4a) Of the above claim(s) *11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicants dated Mar. 4, 2009 have been entered and considered carefully.

Applicants argued again with respect to the restriction requirement and provided no "factual evidence" or "clearly admit in the record" that all combinations of (a-1) to (a-8) and (b-1) to (b-8) is prima facie obvious variation and is considered the same class of compounds. Please note that:

PCT Rule 13.1 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").

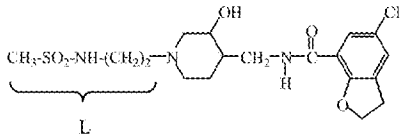
PCT Rule 13.2 states that the unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex B, **Part 1(f)**, indicates the "Markush practice" of alternatives in a single claim. **Part 1(f)I**, indicates the technical relationship and the same or corresponding special technical feature is considered to be met when (A) all alternatives have a common property or activity, and (B) a common structure is present or all alternatives belong to a recognized class of chemical compounds. Further defining (B), Annex B, **Part 1(f)(i-iii)**, the common structure must; a) occupy a large portion of their structure, or b) the common structure constitutes a structurally distinctive portion, or c) where the structures are equivalent and therefore a recognized class of chemical compounds, each member could be substituted for one another with the same intended result. That is, with a common or equivalent structure, there is an expectation relationship and the corresponding special technical feature result from a common (or equivalent) structure that is responsible for the common activity (or property).

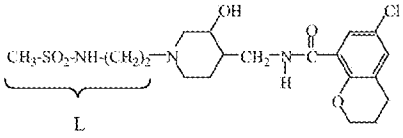
On the contrary to applicants argument, it is evidenced in the art that structurally close related compounds wherein when R1-R2 forms a furanyl ring (a-2), such compounds are 5HT3 antagonists (see CA 127:331398); when R1-R2 forms a pyranyl ring (a-4), such compounds are farnesyltransferase inhibitor (CA134:163037); when R1-R2 forms a methylenedioxy linker (a-1), such compounds have platelet aggregation inhibitory activity (CA146:455250); when R1 and R2

forms a dioxin ring (a-3), such compounds are 5HT4 antagonists. Therefore, ample evidence supporting that the different ring system not only requires tremendous separate searches but also are features corresponding to diversity of utility. Therefore, factual evidence indicated that formula I encompassing (a-1)-(a-8), lacks common or equivalent structure and any expectation in relationship that the corresponding special technical feature result from a common (or equivalent) structure that is responsible for the common activity (or property). In view of the structural diversity, a reference anticipating one group would not necessarily render another group obvious. Therefore, to separately search for such diversity of core structure would be a tremendous burden and restriction is proper.

In addition, were applicants admit in the record that (a-1)-(a-8) are obvious variation, then, the discussion on page 7 of the July 23, 2008 response that compounds 17 and 47 of WO00/37461 as:



compound (17)

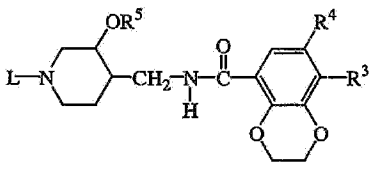


compound (47)

are reverse sulfonamides of the instant claims, then there would have been no patentability of all the claims over WO00/37461, because reverse sulfonamide have been known to be superior structural modification in biologically active compounds (see US 6,888,027).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7, and 10 reading on the elected invention



is continuously prosecuted.

Claims 8-9 have been canceled. Claims 11-13 are withdrawn from consideration per CFR 1.142(b).

2. The rejection of claims 1-7 and 10 under 35 USC 103(a) over Bosmans et al. '997 in view of Lima supplemented with Supuran et al., Chavatte et al. or Penning et al. further in view of Thominet '135 is maintained for reason of record.

Applicants argued that bioisosteric replacement may result in variation in biological activity or selectivity. It is set forth by the court that to establish a case of prima facie obviousness, teaching, suggestion and motivation from the art are the basis and absolute predictability is not required. Ex parte Erlich 3 USPQ2d 1011; In re Pantzer 144 USPQ 415, 419; In re Kronig 190 USPQ 425. In the previous office action, the closest particular species corresponding to the elected species was identified. The specific modification as a design choice of bioisosteric resplacement has been clearly delineated with ample of examples in lead compound modification with reasonable expectation of success.

The employment of a rational design modification using bioisosteric replacement in medicinal chemistry has been well established by the court that such modification of lead compound is indeed prima facie, i.e. see Mead Johnson v Premo Pharm. 207 USPQ 820. The guidelines of finding prima facie obviousness was clearly set forth as (p.830):

> " *Drug design is the attempt by medicinal chemists to plan new chemical structures which will hopefully have improved properties in comparison with prior art drug compounds.*
>
> *One of the methods of drug design is the molecular modification of an existing biologically active compound by changing certain portions of the molecular structure of the original or "lead" compound. The medicinal chemist determines which molecular modifications to attempt based on the experience of other researchers disclosed in the literature of medicinal chemistry and based on the practicalities of carrying out the planned modifications.*
>
> *A skilled medicinal chemist (today as well as in 1955) would not attempt to synthesize a new drug compound through random molecular modification of a lead drug nor would a medicinal chemist review a lead compound atom by atom and systematically attempt various modifications on each of those atoms in order to produce new compounds which then would be tested for their biological activity.*"

Design and skill in bioisosteric replacement has been advanced tremendously since the Mead Johnson decision with conformational and structural analytic information in suggesting many equivalencies as bioisosteric replacements. With respect to the specific CH_3SO_2- and NH_2SO_2- bioisosteres, ample successful examples are evidenced by the Lima , Supuran et al., Chavatte et

al. and Penning et al. reference which particularly described the rational replacement of the sulfonamide linkage.

The compound 103 of the Bosmans et al. '997 has been structurally clear delineated by the reference. On col. 55, table 1, line 63, the biological activity was also disclosed to be good and active. Therefore, compound 103 is a *lead compound*. The modification of a lead compound with rational drug design using a bioisosteric replacement is prima facie obvious with expected variation in activity. In absence of unexpected result, the court has set forth that mere bioisosteric replacement with conventional conformational linkages is prima facie obvious.

3. The provisional rejection of claims 1-7 and 10 under the judicially created doctrine of obviousness type double patenting over SN 10/560,479; 10/560,485 or 10/560,486 in view of Lima supplemented with Supuran, Chavatte or Penning is maintained for reason of record and explaination supra hereby incorporated by reference.

No demarcation among the claims or acceptable terminal disclaimer have been submitted in the record.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Jun. 3, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625